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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/287,377	04/07/1999	ROBERT J. D'AMATO	05213-0272	6240

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EXAMINER
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JONES, DWAYNE C

ART UNIT	PAPER NUMBER
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1614

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/287,377

Applicant(s)

D'AMATO, ROBERT J.

Examiner

Dwayne C Jones

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on the amendment of 24FEB2004.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,7-12,15,19-28,32-39 and 43-48 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,7-12,15,19-28,32-39 and 43-48 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Status of Claims***

1. Claims 1, 7-12, 15, 19-28, 32-39, and 43-48 are pending.
2. Claims 1, 7-12, 15, 19-28, 32-39, and 43-48 are rejected.

### ***Response to Arguments***

3. Applicant's arguments filed February 24, 2004 have been fully considered but they are not persuasive. Applicants present the following arguments. First, applicant purports that the specification describes that diverse pathological states, which are created due to unregulated angiogenesis, are grouped together as angiogenic dependent or angiogenic associated diseases. Second, applicant next alleges that Billson et al. fails to teach or suggest (a) methods comprising the use of compounds recited within the present claims and (b) compositions comprising compounds recited within the present claims. Third, applicant purports that hindsight cannot be used to reject the instant claims. Fourth, applicant submits that the examiner has not provided support for the contention that one having ordinary skill in the art "is provided with the motivation to utilize any angiogenesis agent [sic], which would obviously embrace thalidomide as well as its derivatives and analogue" as well as providing evidence in support of these allegations. Fifth, applicants assert that mere knowledge that certain compounds may allegedly decrease inflammation and/or angiogenesis would not lead one of ordinary skill in the art to applicant's discoveries. Sixth, applicant argues that

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Little II et al. fails to teach of using angiogenesis inhibiting compounds, including thalidomide.

4. First, applicant purports that the specification describes that diverse pathological states, which are created due to unregulated angiogenesis, are grouped together as angiogenic dependent or angiogenic associated diseases. However, this definition is not definitive, and does not provide the artisan with précised definitions and meanings that are embraced by the functional recitations of angiogenic dependent or angiogenic associated diseases. Consequently, this rejection is maintained for both the above-stated and reasons of record.

5. Second, applicant next alleges that Billson et al. fails to teach or suggest (a) methods comprising the use of compounds recited within the present claims and (b) compositions comprising compounds recited within the present claims. Foremost, instant claims 1 and 6-13 are composition claims, which are comprised of two ingredients, (1) a functional recitation of an of angiogenesis inhibitory compound and (2) an anti-inflammatory agent. The prior art reference of Billson et al. teach of treating an inflammatory response in the macula of the eye, namely age-related macular degeneration, with the administration of anti-inflammatory agent, (see abstract). Billson et al. teach that of an example of an anti-inflammatory agent that of steroids, (see pages 2 and 3). From this reference, it is clear that Billson et al. do in fact teach of (a) methods comprising the use of compounds, namely an angiogenesis inhibitory compound (thalidomide) and an anti-inflammatory agent (steroid) recited within the

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present claims and (b) compositions of these compounds, as recited within the present claims.

6. Thirdly in response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). The skilled artisan would have been motivated from the combined prior art teachings of Oliver et al. in view of either Willoughby et al. of WO 94/23725 possessing a publication date of October 27, 1994 or Collville-Nash et al. of making a composition that is comprised of the functional recitation of angiogenesis inhibitory compound and an anti-inflammatory agent. "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. . . . [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). In addition, the instant rejection is over the combined teachings of either (1) of Oliver et al. in view of Willoughby et al. of WO 94/23725 or (2) of Oliver et al. in view of Collville-Nash et al. For these reasons, these prior art references teach of elements that are comprised of the instant claims.

7. Fourth, applicant submits that the examiner has not provided support for the contention that one having ordinary skill in the art "is provided with the motivation to utilize any angiogenesis agent [sic], which would obviously embrace thalidomide as well as its derivatives and analogues." It is surely within the level of the skilled artisan to utilize derivatives and analogues of a compound such as thalidomide as long as the inherent properties of a given compound, such as thalidomide, are not materially changed. Accordingly, it would have been obvious to one having ordinary skill in the art to include various iterations and derivatives of known compounds when the prior art teaches that a compound, namely thalidomide, is used to treat the very same ailment, such as macular degeneration, that is claimed. Moreover, applicant requests documentation of well-known cyclization reactions between carboxylic acids and carboxylic acid amide functional groups. Lactones are carboxylic acids that have hydroxyl groups on a gamma or delta carbon atom (3 or 4, respectively carbons away from the carboxylic acid moiety group), which may undergo intramolecular esterification to give a cyclic ester, (see pages 799-800 of Solomons, 3<sup>rd</sup> Edition, Organic Chemistry, 1986). Likewise, lactams are structurally related to lactones with the exception of having an internal carboxylic acid amidyl moiety in lieu of the carboxylic acid ester moiety as in a lactone, (see pages 799, 800, and 806 of Solomons, 3<sup>rd</sup> Edition, Organic Chemistry, 1986). Consequently, compounds with carboxylic acids that have amino groups on a gamma or delta carbon atom would also undergo intramolecular cyclization reactions, thus generating lactams. In addition, various iterations of carboxylic acids and its corresponding derivatives, namely amides, anhydrides, halides, can readily

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undergo internal cyclization reactions as the distance between carboxylic acid functional group increases between a functional groups such as hydroxyl, amino, or another carboxylic acid moiety, (for instance see page 802 cyclic anhydrides are reacted with ammonia or an amine while heating to generate cyclic imides). Accordingly, internal cyclization reactions are clearly obvious to one having ordinary skill in the art as evidenced by Solomons, 3<sup>rd</sup> Edition, Organic Chemistry, 1986. Even though the instant claims may exclude the compound of thalidomide one having ordinary skill in the art has the knowledge to generate and recognize derivatives and precursors of compounds through basic organic chemistry. Compounds such as P, Q, R, or S could readily undergo internal cyclization reactions under the right conditions, and the skilled artisan would readily discern and recognize precursors of such compounds as obvious variants of a known compound, especially the very well known compound of thalidomide.

8. Fifth, applicants assert that mere knowledge that certain compounds may allegedly decrease inflammation and/or angiogenesis would not lead one of ordinary skill in the art to applicant's discoveries. However, the prior art reference of Billson et al. clearly and specifically teach of administering thalidomide and a steroid, namely triamcinolone acetonide is used to treat macular degeneration, (see page 4, lines 11-19). From these teachings of Billson et al., one having ordinary skill in the art is provided with clear motivation to make a composition that is comprised of thalidomide and a steroid as well as methods of using these compositions to treat the claimed ailment, such as macular degeneration.

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9. Sixth, applicant argues that Little II et al. fails to teach of using angiogenesis inhibiting compounds, including thalidomide. The examiner agrees with this statement. However, Billson et al. do in fact teach of methods of using compounds, namely an angiogenesis inhibitory compound (thalidomide) and an anti-inflammatory agent (steroid). The rejection is not over Little II et al. by itself, but rather Billson et al. in view of Little II et al. Accordingly, Little II et al. teaches the skilled artisan that other ailments can be treated when angiogenesis is modulated. The skilled artisan would have been motivated to treat other ailments that result from neovascularization or angiogenesis.

***Claim Rejections - 35 USC § 112***

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1, 7-12, 15, 19-28, 32-39, and 43-48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treating the diseases of corneal neovascularization and Crohn's Disease, and V2-carcinoma, does not reasonably provide enablement for "inhibiting angiogenesis" and "treating angiogenesis dependent disease". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

12. The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re

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Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The instant invention is directed to angiogenic compositions and methods of treating angiogenesis dependant diseases. The method comprises administering angiogenic inhibiting compound and an anti-inflammatory agent.

(1) The state of the prior art:

The compounds of the inventions are angiogenic compositions and methods of treating angiogenesis dependant diseases with the administration of angiogenic inhibiting compound and an anti-inflammatory agent, whereas the prior art of Billson et al. of WO 95/03807 only teaches of treating macular degeneration.

(3) The relative skill of those in the art

The relative skill of those in the art of pharmaceuticals is high.

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## (4) The predictability or unpredictability of the art

The unpredictability of the pharmaceutical art is very high. In fact, the courts have made a distinction between mechanical elements function the same in different circumstances, yielding predictable results, chemical and biological compounds often react unpredictably under different circumstances. Nationwide Chem. Corp. v. Wright, 458 F. Supp. 828, 839, 192 USPQ 95, 105(M.D. Fla. 1976); Aff'd 584 F.2d 714, 200 USPQ 257 (5<sup>th</sup> Cir. 1978); In re Fischer, 427 F.2d 833, 839, 166 USPQ 10, 24 (CCPA 1970). Thus, the physiological activity of a chemical or biological compound is considered to be an unpredictable art. For example, in Ex Parte Sudilovsky, the Court held that Appellant's invention directed to a method for preventing or treating a disease known as tardive dyskinesia using an angiotensin converting enzyme inhibitor involved unpredictable art because it concerned the pharmaceutical activity of the compound. 21 USPQ2d 1702, 1704-5 (BDAI 1991); In re Fisher, 427 F.2d 1557, 1562, 29 USPQ, 22 (holding that the physiological activity of compositions of adrenocorticotrophic hormones was unpredictable art); In re Wright, 999 F.2d 1557, 1562, 29 USPQ d, 1570, 1513-14 (Fed. Cir. 1993) (holding that the physiological activity of RNA viruses was unpredictable art); Ex Parte Hitzeman, 9 USPQ2d 1821, 1823 (BDAI 1987); Ex Parte Singh, 17 USPQ2d 1714, 1715, 1716 (BPAI 1990). Likewise, the physiological or pharmaceutical activity of angiogenesis inhibitory composition for the treatment of angiogenesis dependent diseases prior to filing of the instant invention was an unpredictable art.

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## (5) The breadth of the claims

The instant claims are very broad. For instance, claim 1 is directed to the plethora of compounds that are embraced by the functional recitation of simply being known as an “angiogenesis inhibiting compound and an anti-inflammatory drug”. The breadth of claims was a factor in Amgen v. Chugai Pharm. Co., 927 F.2d 1200, 18 USPQ2d (Fed. Cir.), cert. Denied, 502 U.S. 856 (1991). In the Amgen case, the patent claims were directed to DNA sequences that encoded amino acid sequences. Because a very small change in the amino acid sequence of a protein can result in a very large change in the structure-function activity of a protein and because the laws of protein folding are in such a primitive state, predicting protein structure (and hence, activity) while knowing only the sequence of the protein is akin to predicting the weather for a date in the future.

## (6) The amount of direction or guidance presented

The amount of guidance or direction needed to enable the invention is inversely related to the degree of predictability in the art. In re Fisher, 839, 166 USPQ 24. Thus, although a single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements, in cases involving unpredictable factors, such as most chemical reactions and physiological activity, more teaching or guidance is required. In re Fischer, 427 F.2d 839, 166 USPQ 24; Ex Parte Hitzeman, 9 USPQ 2d 1823. For example, the Federal Circuit determined that, given the unpredictability of the physiological activity of RNA viruses, a specification requires

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more than a general description and a single embodiment to provide an enabling disclosure for a method of protecting an organism against RNA viruses. In re Wright, 999 F.2d 1562-63, 27 USPQ2d 1575. In the instant case, given the unpredictability of the physiological or pharmaceutical activity of a compounds that are embraced by the functional recitation of simply being known as an "angiogenesis inhibiting compound and an anti-inflammatory drug" to be effective in treating angiogenesis dependent diseases is insufficient for enablement. The specification provides no guidance, in the way of enablement for compounds that are embraced by the functional recitation of simply being known as an "angiogenesis inhibiting compound and an anti-inflammatory drug" other than the diseases of corneal neovascularization and Crohn's Disease, and V2-carcinoma, (see pages 33-40 of the instant specification). In addition, the specification does not provide any enablement of derivatives or analogues of angiogenesis inhibiting compounds that could be employed in this invention other than thalidomide, EM-12, PGA, PG Acid and supidimide along with sulindac and only for the treatment of the diseases of corneal neovascularization and Crohn's Disease, and V2-carcinoma. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also In re Wright, 999 F.2d 1557, 27 USPQ2d 1510 (Fed. Cir. 1993); In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work. In re Dreshfield, 110 F.2d 235, 45 USPQ 36 (CCPA 1940), gives this general rule: "It is well settled that in cases involving chemicals and chemical compounds, which differ radically in their properties it

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must appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical combinations included in the claims are capable of accomplishing the desired result." The article "Broader than the Disclosure in Chemical Cases," 31 J.P.O.S. 5, by Samuel S. Levin covers this subject in detail. A disclosure should contain representative examples, which provide reasonable assurance to one skilled in the art that the compounds fall within the scope of a claim will possess the alleged activity. See In re Riat et al. (CCPA 1964) 327 F2d 685, 140 USPQ 471; In re Barr et al. (CCPA 1971) 444 F 2d 349, 151 USPQ 724.

(7) The presence or absence of working examples

As stated above, the specification discloses the angiogenesis inhibiting compounds that have the purported ability to treat a variety of diseases that are known functionally as angiogenesis dependent diseases. However, the instant specification only has enablement for angiogenesis inhibiting compounds that could be employed in this invention other than thalidomide, EM-12, PGA, PG Acid and supidimide along with sulindac and only for the treatment of the diseases of corneal neovascularization and Crohn's Disease, and V2-carcinoma, (see pages 33-40 of the instant specification).

(8) The quantity of experimentation necessary

The quantity of experimentation needed to be performed by one skilled in the art is yet another factor involved in the determining whether "undue experimentation" is

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required to make and use the instant invention. "The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." In re Wands, 858 F.2d 737, 8 USPQ2d 1404 (citing In re Angstadt, 537 F.2d 489, 502-04, 190 USPQ 214, 218 (CCPA 1976)). For these reasons, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to determine all of the angiogenesis inhibiting compounds as well as the litany of ailments that are embraced by the phrase "angiogenesis dependent disease" that would be enabled in this specification.

13. The rejection of claims 19, 20, 27, 28, 37-39, and 48 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained and repeated. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained. There is insufficient descriptive support for the phrase "treating angiogenesis dependent disease". In addition, the instant specification does not describe what is meant by the phrase "treating angiogenesis dependent disease". Structural identifying characteristics of the phrase "treating angiogenesis dependent disease". There is no evidence that there is any per se structure/function relationship between the phrase "treating angiogenesis dependent disease". The instant specification does provide an adequate written description for the phrase "treating

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angiogenesis dependent disease". Accordingly, these claims fail to comply with the written description requirement.

14. Claims 15, 19, 20, 45, and 46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

15. *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997), cert. denied, 523 U.S. 1089, 118 S.Ct. 1548 (1980), holds that an adequate written description requires a precise definition, such as by structure, formula, chemical name, or physical properties, "not a mere wish or plan for obtaining the claimed chemical invention." *Eli Lilly*, 119 F.3d at 1566. The Federal Circuit has adopted the standard set forth in the Patent and Trademark Office ("PTO") Guidelines for *Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement ("Guidelines")*, 66 Fed. Reg. 1099 (Jan. 5, 2001), which state that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics, "including, inter alia, "functional characteristics when coupled with a known or disclosed correlation between function and structure...." *Enzo Biochem, Inc. v. Gen-Probe.*, 296 F.3d, 316, 1324-25 (Fed. Cir. 2002) (quoting Guidelines, 66 Fed. Reg. At 1106 (emphasis added)). Moreover, although *Eli Lilly* and *Enzo* were decided within the factual context of DNA sequences, this does not preclude extending the reasoning of those cases to chemical

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structures in general. *Univ. of Rochester v. G.D. Searle & Co.*, 249 F. Supp.2d 216, 225 (W.D.N.Y 2003).

16. There is insufficient descriptive support for the phrase "angiogenesis inhibitory compound". In addition, the instant specification does not describe what is meant by the phrase "angiogenesis inhibitory compound". Structural identifying characteristics of the phrase "angiogenesis inhibitory compound". There is no evidence that there is any per se structure/function relationship between the phrase "angiogenesis inhibitory compound". other than those disclosed, namely the compounds of formulas A, B, and C as identified in claim 7. The instant specification does provide an adequate written description for the phrase "angiogenesis inhibitory compound". The instant specification does not adequately provide one skilled in the art with clear definitions not to mention assays to determine what and how a compound is determined to be angiogenesis inhibitory composition. Accordingly, these claims fail to comply with the written description requirement.

17. The rejections of claims 7, 9, 12, 26, and 27 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in response to the amendment of February 24, 2004.

***Claim Rejections - 35 USC § 103***

18. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

19. The rejection of claims 1, 7-12, 15, 19-28, 32-39, and 43-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oliver et al. in view of either Willoughby et al. of WO 94/23725 possessing a publication date of October 27, 1994 or Collville-Nash et al. is maintained for the reasons cited previously and above.

20. The rejection of claims 1, 7-12, 15, 19-28, 32-39, and 43-48 under 35 U.S.C. 103(a) as being unpatentable over Billson et al. of WO 95/03807 is maintained for reasons cited previously and above.

21. The rejection of claims 1, 7-12, 15, 19-28, 32-39, and 43-48 under 35 U.S.C. 103(a) as being unpatentable over Billson et al. of WO 95/03807 in view of Little, II et al of U.S. Patent No. 5,348,942 is also maintained for both the above-stated and reasons of record.

22. The rejection of claims 9-12 under 35 U.S.C. 103(a) as being unpatentable over Billson et al. of WO 95/03807 in view of Little, II et al of U.S. Patent No. 5,348,942 is maintained for the reasons of record and those stated above.

***Obviousness-type Double Patenting***

23. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA

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1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

24. The provisional rejection of claims 1, 7-12, 15, 19-28, 32-39, and 43-48 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 7-12, 15, 19-39, and 43-48 of copending Application No. 09/287,377 is maintained and repeated. Although the conflicting claims are not identical, they are not patentably distinct from each other because both are directed to compositions and methods of treating and or inhibiting angiogenesis as well as angiogenesis dependent diseases.

25. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

26. Claims 1, 7-12, 15, 19-28, 32-39, and 43-48 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of copending Application No. 09/480,448. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant invention and the copending Application No. 09/480,448 teach of compositions of angiogenesis containing compounds and anti-inflammatory drugs as well as methods of employing these compounds to treat similar ailments.

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27. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

28. Claims 1, 7-12, 15, 19-28, 32-39, and 43-48 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of copending Application No. 10/430,892. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant invention and the copending Application No. 10/430,892 teach of compositions of angiogenesis containing compounds and anti-inflammatory drugs as well as methods of employing these compounds to treat similar ailments..

29. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. C. Jones whose telephone number is (571) 272-0578. The examiner can normally be reached on Mondays, Tuesdays, Thursday, and Fridays from 8:30 am to 6:00 pm.

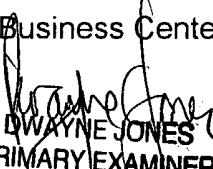
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, may be reached at (571) 272-0951. The official fax No. for correspondence is (703) 872-9306.

Also, please note that U.S. patents and U.S. patent application publications are no longer supplied with Office actions. Accordingly, the cited U.S. patents and patent application publications are available for download via the Office's PAIR, see <http://pair->

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direct.uspto.gov. As an alternate source, all U.S. patents and patent application publications are available on the USPTO web site (www.uspto.gov), from the Office of Public Records and from commercial sources.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see http://pair-direct.uspto.gov Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 1-866-217-9197 (toll free).

  
DWAYNE JONES  
PRIMARY EXAMINER  
Tech. Ctr. 1614  
September 15, 2004